

New Approach Methodologies: Translational Impact and Human Relevance of Microphysiological Systems

- **Introduction**

Presenter: Dr. Brian Berridge, NIEHS/NTP

An aspiration to move toxicology from a predominately observational science to one that can reasonably predict human outcomes from more fundamental mechanistic bioactivity information has successfully instigated the generation of a significant volume of that mechanistic information. Turning that information into decisional understandings of health effects has been a bit more of a challenge. We have likely under-estimated our ability to link bioactivities in very simple biological systems to outcomes in very complex biological systems. Human-derived microphysiological systems could be an important bridge between these two ends of the biological spectrum. Building the bridge will take more than building the assay systems. It will require a clear understanding of the questions we're aiming to answer and even a recognition that those questions will be different than those you would ask in a high throughput bioactivity assay or an in vivo animal study.

- **The NIH Microphysiological Systems Program: Tissue Chips for Drug Safety and Efficacy Studies**

Presenters: Dr. Danilo Tagle and Dr. Lucie Low, National Center for Advancing Translational Sciences

The NIH Microphysiological Systems (Tissue Chips) program led by NCATS is developing alternative approaches for more reliable readouts of toxicity and efficacy during drug development. Tissue chips are microfluidic cell culture systems utilizing human primary or stem cells seeded in bioengineered platforms that mimic tissue histoarchitecture and function of human organs. Presentation will describe platforms for safety applications, for disease modeling, and how independent validation centers are helping to build confidence in these systems. Effective partnerships with stakeholders and future initiatives will also be presented towards widespread adoption of this emerging technology.

- **Advancing Regulatory Science by Innovation – In Vitro Microphysiological Systems**

Presenter: Suzanne Fitzpatrick, PhD, DABT, ERT, U.S. Food and Drug Administration

FDA has formed a FDA Senior Toxicologist Working Group to share information on new toxicology methods and to familiarize FDA regulatory and research scientists on emerging toxicology tests and their usefulness in risk assessment. FDA Commissioner Gottlieb tasked FDA's Toxicology Working Group with the development of a FDA Predictive Toxicology Roadmap for integrating emerging predictive toxicology methods and new technologies into regulatory risk assessments. The roadmap was presented in December 2017 and a public meeting was held on September 2018. FDA listened to input from this public meeting and responded to stakeholders' comments. FDA formed

an In Vitro Systems Work Group (IVSWG) and will be looking at In Vitro Microphysiological Systems (MPS) as its first activity. FDA has several different MPS chips in FDA laboratories. This research will enable FDA scientists to contribute to the development of performance criteria for MPS. FDA will also be developing a Request for Information on MPS and a seminar series for developers to present their new in vitro technologies to FDA scientists.

- **Beyond 3D-models – Building Confidence in Microphysiological Models**

Presenter: Dr. Szczepan Baran, Novartis

Microphysiological Systems (MPS) have a potential to impact various stages of drug development including efficacy and safety. There is a significant amount of hype regarding this technology that exceeds what is currently technically and biologically feasible. While there has been an enormous amount of progress in this field, the technology is still in its infancy and requires characterization, validation and optimization before we can fully understand its potential. During this session, an overview of the current state and realistic possibilities of MPS technology will be provided.